

including January 21, 2001, and have paid the requisite fee [37 C.F.R. §§ 1.136(a), 1.17(a)(3)].

Kindly amend the application as follows:

IN THE CLAIMS:

Please cancel claims 51 to 75, without prejudice.

Please add claims 76 to 102 as follows:

76. An HLA-DR typing process comprising the steps of:  
(a) hybridizing DNA in a sample to be typed to a DNA sequence, said DNA sequence being capable of hybridizing to a polymorphic region of an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex to allow determination of one or more HLA-DR alleles, said polymorphic region being encoded by a DNA sequence selected from the group consisting of:

- (i) DNA sequences encoding amino acids 8-14 of said locus;
- (ii) DNA sequences encoding amino acids 26-32 of said locus;
- (iii) DNA sequences encoding amino acids 72-78 of said locus;
- (iv) DNA sequences which are allelic variants of any of the foregoing DNA sequences; and

- (v) DNA sequences which are fully complementary to any of the foregoing DNA sequences, and
- (b) detecting areas of hybridization between said DNA in said sample and said DNA sequence.

77. An HLA-DR typing process comprising the steps of:

- (a) restricting a first DNA isolated from an individual to be typed with at least one restriction endonuclease;
- (b) size-fractionating said restricted DNA;
- (c) hybridizing said size-fractionated DNA to be typed to a second DNA, said second DNA being capable of hybridizing to a polymorphic region of an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex to allow determination of one or more HLA-DR alleles, said polymorphic region being encoded by a DNA sequence selected from the group consisting of:
- (i) DNA sequences encoding amino acids 8-14 of said locus;
- (ii) DNA sequences encoding amino acids 26-32 of said locus;
- (iii) DNA sequences encoding amino acids 72-78 of said locus;

(iv) DNA sequences which are allelic variants of any of the foregoing DNA sequences; and

(v) DNA sequences which are fully complementary to any of the foregoing DNA sequences, and

(d) detecting areas of hybridization between said size-fractionated DNA and said second DNA.

78. An HLA-DR typing process comprising the steps of:

(a) hybridizing DNA in a sample to be typed to a DNA sequence, said DNA sequence being capable of hybridizing to a polymorphic region of an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex to allow determination of one or more HLA-DR alleles, said polymorphic region being encoded by a DNA sequence selected from the group consisting of:

(i) DNA sequences encoding a majority of the amino acid sequence in a region consisting essentially of amino acids 8-14, 26-32 or 72-78 of a polypeptide sequence coded for by DNA insert DR- $\beta$ -A, DR- $\beta$ -B or DR- $\beta$ -C;

(ii) DNA sequences which are allelic variants of any of the foregoing DNA sequences; and

- (iii) DNA sequences which are fully complementary to any of the foregoing sequences, and
- (b) detecting areas of hybridization between said DNA in said sample and said DNA sequence.

79. An HLA-DR typing process comprising the steps of:

- (a) restricting a first DNA isolated from an individual to be typed with at least one restriction endonuclease;
- (b) size-fractionating said restricted DNA;
- (c) hybridizing said size-fractionated DNA to be typed to a second DNA, said second DNA being capable of hybridizing to a polymorphic region of an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex to allow determination of one or more HLA-DR alleles, said polymorphic region being encoded by a DNA sequence selected from the group consisting of:

- (i) DNA sequences encoding a majority of the amino acid sequence in a region consisting essentially of amino acids 8-14, 26-32 or 72-78 of a polypeptide sequence coded for by DNA insert DR- $\beta$ -A, DR- $\beta$ -B or DR- $\beta$ -C;

(ii) DNA sequences which are allelic variants of any of the foregoing DNA sequences; and

(iii) DNA sequences which are fully complementary to any of the foregoing sequences, and

(d) detecting areas of hybridization between said size-fractionated DNA and said second DNA.

80. An HLA-DR typing process comprising the steps of:

(a) hybridizing DNA in a sample to be typed to a DNA sequence, said DNA sequence being selected from the group consisting of:

(i) GGGGACACCCGACCACGTTCTTGGAGCTGCTTAAGTCTGAG  
TGTCAATTCTCAATGGGACGGAGCGGGTGCCTGGAGA  
GACACTTCCATAACCAGGAGGAGTACGCGCGCTCGACAGCG  
ACGTGGGGAGTACCGGGCGGTGAGGGAGCTGGGGCGGCCTG  
ATGCCGAGTACTGGAACAGCCAGAAGGACCTCCTGGAGCAGA  
AGCGGGGCCAGGTGGACAATTACTGCAGACACAACACTACGGGGTTG  
TGGAGAGCTTCACAGTGAGCGGGAGTCCATCCTCAGGTGACTG  
TGTATCCTGCAAGACCCAGCCCCTGCAGCACCACAAACCTCCTGGT  
CTGCTCTGTGAGTGGTTCTATCCAGGCAGCATTGAAGTCAGTGG

TTCCGGAACGCCAGGAAGAGAAGGGCTGGGTGGTCCACGGC  
CTGATCCAGAATGGAGACTGGACCTCCAGACCTGGTATGCTA  
GAAACATTCCTCGGAGTGGAGAGGTTACACCTGCCAAGTGGAG  
CACCCAAGCGTAACGAGCCCTCTCACAGTGGATGGAGTGCACGG  
TCTGAATCTGCACAGAGCAAGATGCTGAGTGGAGTCGGGGCTTT  
GTGCTGGGCCTGCTCTCCTGGGGCGGGCTGTTCATCTACTTC  
AGGAATCAGAAAGGACACTCTGGACTTCAGCCAACAGGATTCTG  
AGC;

(ii) GGGGACACCCGACCACGTTCTGGAGCAGGTTAACATGAGTGT  
CATTCTTCAACGGACGGAGCGGGTGCCTGGACAGATAAC  
TTCTATCACCAAGAGGAGTACGTGCGCTCGACAGCGACGTGGGG  
GAGTACCGGGCGTGACGGAGCTGGGGCGGCCTGATGCCGAGTAC  
TGGAACAGCCAGAAGGACCTCCTGGAGCAGAAGCGGGCCGGTG  
GACACCTACTGCAGACACAACACTACGGGGTTGGTGAGAGCTTCACA  
GTGCAGCGCGAGTCTATCCTGAGGTGACTGTGTATCCTGCAAAG  
ACCCAGCCCCTGCAGCACACAAACCTCCTGGTCTGCTCTGTGAAT  
GGTTTCTATCCAGGCAGCATTGAAGTCAGGTGGTCCGGAACGGC  
CAGGAAGAGAAGACTGGGGTGGTCCACAGGCCTGATCCAGAAT  
GGAGACTGGACCTCCAGACCCCTGGTATGCTGGAAACAGTCCT  
CGGAGTGGAGAGGTTACACCTCCAAGTGGAGCACGGTCTGAATCTGCA  
ACGAGCCCTCTCACAGTGGATGGAGAGCACGGTCTGAATCTGCA  
CAGAGCAAGATGCTGAGTGGAGTCGGGGCTCGTGTGGCCTG  
CTCTTCCCTGGGGCCGGGCTGTTCATCTACTTCAGGAATCAG

AAAGGACACTCTGGACTTCAGCCAACAGGATTCTGAGC;

(iii) a DNA sequence which is fully complementary to the DNA sequence of (I) or (ii); and

(iv) a DNA sequence which differs from the DNA sequence of (I) or (ii) in codon sequence due to the degeneracy of the genetic code, and

(b) detecting areas of hybridization between said DNA in said sample and said DNA sequence.

81. An HLA-DR typing process comprising the steps of:

(a) restricting a first DNA isolated from an individual to be typed with at least one restriction endonuclease;

(b) size-fractionating said restricted DNA;

(c) hybridizing said size-fractionated DNA to be typed to a second DNA, said second DNA being selected from the group consisting of:

(i) GGGGACACCCGACCACGTTCTTGGAGCTGCTTAAGTCTGAG  
TGTCATTTCTCAATGGGACGGAGCGGGTGCCTGGAGA  
GACACTTCCATAACCAGGAGGAGTACGCGCGCTTCGACAGCG  
ACGTGGGGAGTACCGGGCGGTGAGGGAGCTGGGGCGGCCTG  
ATGCCGAGTACTGGAACAGCCAGAAGGACCTCCTGGAGCAGA

AGCGGGGCCAGGTGGACAATTACTGCAGACACAACACTACGGGGTTG  
TGGAGAGCTTCACAGTGCAGCGCGAGTCCATCCTCAGGTGACTG  
TGTATCCTGCAAGACCCAGCCCCGCAGCACCACAACCTCCTGGT  
CTGCTCTGTGAGTGGTTCTATCCAGGCAGCATTGAAGTCAGTGG  
TTCCGGAACGGCCAGGAAGAGAAGGCTGGGTGGTCCACGGC  
CTGATCCAGAACGGAGACTGGACCTCCAGACCCCTGGTATGCTA  
GAAACATTCCTCGGAGTGGAGAGGTTACACCTGCCAAGTGGAG  
CACCCAAGCGTAACGAGCCCTCTCACAGTGGAAATGGAGTGCACGG  
TCTGAATCTGCACAGAGCAAGATGCTGAGTGGAGTCGGGGCTTT  
GTGCTGGGCCTGCTCTCCTGGGGCCGGCTGTTCATCTACTTC  
AGGAATCAGAAAGGACACTCTGGACTTCAGCCAACAGGATTCTG  
AGC;

(ii) GGGGACACCCGACCACGTTCTTGGAGCAGGTTAACATGAGTGT  
CATTTCTTCAACGGGACGGAGCAGGGTGGCTGGACAGATA  
TTCTATCACCAAGAGGAGTACGTGCGCTCGACAGCGACGTGGGG  
GAGTACCGGGCGTGACGGAGCTGGGGCGGCCTGATGCCAGTAC  
TGGAACAGCCAGAAGGACCTCCTGGAGCAGAACGGGCCGCGGTG  
GACACCTACTGCAGACACAACACTACGGGGTTGGTGGAGAGCTTCACA  
GTGCAGCGCGAGTCTATCCTGAGGTGACTGTGTATCCTGCAAAG  
ACCCAGCCCCCTGCAGCACCACAACCTCCTGGTCTGCTCTGTGAAT  
GGTTTCTATCCAGGCAGCATTGAAGTCAGGTGGTCCACAGGCCTGATCCAGAAT  
CAGGAAGAGAAGACTGGGGTGGTCCACAGGCCTGATCCAGAAT  
GGAGACTGGACCTCCAGACCCCTGGTGGTGTGCTGGAAACAGTTCCT

CGGAGTGGAGAGGTTTACACCTCCCAAGTGGAGCACCCAAGCCTG  
ACGAGCCCTCTCACAGTGGATGGAGAGCACGGTCTGAATCTGCA  
CAGAGCAAGATGCTGAGTGGAGTCGGGGCTTCGTGCTGGCCTG  
CTCTCCTGGGGCCGGCTGTTCATCTACTTCAGGAATCAG  
AAAGGACACTCTGGACTTCAGCCAACAGGATTCTGAGC;

- (iii) a DNA sequence which is fully complementary to the DNA sequence of (I) or (ii); and
- (iv) a DNA sequence which differs from the DNA sequence of (I) or (ii) in codon sequence due to the degeneracy of the genetic code,  
and

(d) detecting hybridization between said size-fractionated DNA and said second DNA.

82. An HLA-DR typing process comprising the steps of:

- (a) hybridizing DNA in a sample to be typed to a DNA sequence, said DNA sequence being capable of hybridizing to a constant region of an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex, said constant region being encoded by a DNA sequence selected from the group consisting of:

- (i) DNA sequences encoding amino acids 39-45 of said locus; and

(ii) DNA sequences which are fully complementary to any of the foregoing DNA sequences, and

(b) detecting areas of hybridization between said DNA in the sample and said DNA sequence.

83. An HLA-DR typing process comprising the steps of:

(a) restricting a first DNA isolated from an individual to be typed with at least one restriction endonuclease;

(b) size-fractionating said restricted DNA;

(c) hybridizing said size-fractionated DNA to be typed to a second DNA, said second DNA being capable of hybridizing to a constant region of an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex, said constant region being encoded by a DNA sequence selected from the group consisting of:

(i) DNA sequences encoding amino acids 39-45 of said locus; and

(ii) DNA sequences which are fully complementary to any of the foregoing DNA sequences, and

(d) detecting areas of hybridization between said size-fractionated DNA and said second DNA.

84. An HLA-DR typing process comprising the steps of:

(a) hybridizing DNA in a sample to be typed to a DNA sequence, said DNA sequence being capable of hybridizing to a constant region of an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex, said constant region being encoded by a DNA sequence selected from the group consisting of:

(i) DNA sequences encoding a majority of the amino acid sequence in a region consisting essentially of amino acids 39-45 of a polypeptide sequence coded for by DNA insert DR- $\beta$ -A, DR- $\beta$ -B or DR- $\beta$ -C; and

(ii) DNA sequences which are fully complementary to any of the foregoing sequences, and

(b) detecting areas of hybridization between said DNA in the sample and said DNA sequence.

85. An HLA-DR typing process comprising the steps of:

(a) restricting a first DNA isolated from an individual to be typed with at least one restriction endonuclease;

(b) size-fractionating said restricted DNA;

(c) hybridizing said size-fractionated DNA to be typed to a second DNA, said second DNA being capable of hybridizing to a constant region of an HLA-DR- $\beta$  chain locus of the human

lymphocyte antigen complex, said constant region being encoded by a DNA sequence selected from the group consisting of:

- (i) DNA sequences encoding a majority of the amino acid sequence in a region consisting essentially of amino acids 39-45 of a polypeptide sequence coded for by DNA insert DR- $\beta$ -A, DR- $\beta$ -B or DR- $\beta$ -C; and
- (ii) DNA sequences which are fully complementary to any of the foregoing sequences, and

(d) detecting areas of hybridization between said DNA to be typed and said second DNA.

86. The HLA-DR typing process according to claim 76 or 78, wherein said DNA sequence is characterized by a nucleotide sequence selected from the group consisting of:

TGGAGCTGCTTAAGTCTGA, TCCTGGAGAGACACTTCCA,  
GGGGCCAGGTGGACAATTA, TGGAGCAGGTTAACATGA, TCCTGGACAGATACTTCTA  
and GGGCCGCGGTGGACACCTA.

87. The HLA-DR typing process according to claim 77 or 79, wherein said second DNA is characterized by a nucleotide sequence selected from the group consisting of:

TGGAGCTGCTTAAGTCTGA, TCCTGGAGAGACACTTCCA, GGGGCCAGGTGGACAATTA,  
TGGAGCAGGTTAACATGA, TCCTGGACAGATACTTCTA and GGGCCGCGGTGGACACCTA.

88. The HLA-DR typing process according to any one of claims 76, 78, 80, 82 or 84, further comprising the step of comparing said hybridization to hybridization between DNA of known HLA-DR type and said DNA sequence.

89. The HLA-DR typing process according to any one of claims 77, 79, 81, 83 or 85, further comprising the step of comparing said hybridization to hybridization between DNA of known HLA-DR type and said second DNA.

90. The HLA-DR typing process according to any one of claims 76, 78, 80, 82 or 84, wherein prior to the step of detecting said areas of hybridization, the process further comprises the step of hybridizing said DNA in said sample to a hybridization control, said hybridization control being a DNA having the nucleotide sequence: GCTTCGACAGCGACGTGGG.

91. The HLA-DR typing process according to any one of claims 77, 79, 81, 83 or 85, wherein prior to the step of detecting said areas of hybridization, the process further

comprises the step of hybridizing said size-fractionated DNA to a hybridization control, said hybridization control being a DNA having the nucleotide sequence: GCTTCGACAGCGACGTGGG.

92. The HLA-DR typing process according to any one of claims 76, 78, 80, 82 or 84, wherein said DNA sequence is a labeled DNA sequence and its label is used for detecting hybridization between said DNA in said sample and said DNA sequence.

93. The HLA-DR typing process according to any one of claims 77, 79, 81, 83 or 85, wherein said second DNA is a labeled DNA and its label is used for detecting hybridization between said size-fractionated DNA and said second DNA.

94. An HLA-DR typing kit comprising a DNA sequence selected from the group consisting of:

- (i) DNA sequences encoding amino acids 8-14 of an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex;
- (ii) DNA sequences encoding amino acids 26-32 of an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex;

- (iii) DNA sequences encoding amino acids 72-78 of an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex;
- (iv) DNA sequences which are allelic variants of any of the foregoing DNA sequences; and
- (v) DNA sequences which are fully complementary to any of the foregoing DNA sequences.

95. An HLA-DR typing kit comprising a DNA sequence which hybridizes to an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex, said DNA sequence being capable of hybridizing to a polymorphic region of said locus to allow determination of one or more HLA alleles for use in HLA-DR- $\beta$  typing, said polymorphic region being encoded by a DNA sequence selected from the group consisting of:

- (i) DNA sequences encoding amino acids 8-14 of said locus;
- (ii) DNA sequences encoding amino acids 26-32 of said locus;
- (iii) DNA sequences encoding amino acids 72-78 of said locus;
- (iv) DNA sequences which are allelic variants of any of the foregoing DNA sequences; and

(v) DNA sequences which are fully complementary to any of the foregoing DNA sequences.

96. An HLA-DR typing kit comprising a DNA sequence which hybridizes to an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex, said DNA sequence being capable of hybridizing to a polymorphic region of said locus to allow determination of one or more HLA alleles for use in HLA-DR- $\beta$  typing, said polymorphic region being encoded by a DNA sequence selected from the group consisting of:

(i) DNA sequences encoding a majority of the amino acid sequence in a region consisting essentially of amino acids 8-14, 26-32 or 72-78 of a polypeptide sequence coded for by DNA insert DR- $\beta$ -A, DR- $\beta$ -B or DR- $\beta$ -C;

(ii) DNA sequences which are allelic variants of any of the foregoing DNA sequences; and

(iii) DNA sequences which are fully complementary to any of the foregoing sequences.

97. The HLA-DR typing kit according to any one of claims 94, 95 or 96, wherein said DNA sequence is labeled.

98. The HLA-DR typing kit according to any one of claims 94, 95 or 96, further comprising a 19-mer hybridization control, said hybridization control being a DNA having the nucleotide sequence: GCTTCGACAGCGACGTGGG.

99. An HLA-DR typing kit comprising a DNA sequence selected from the group consisting of:

- (i) DNA sequences encoding amino acids 39-45 of an HLA-DR- $\beta$  locus of the human lymphocyte antigen complex, and
- (ii) DNA sequences which are fully complementary to any of the foregoing DNA sequences.

100. An HLA-DR typing kit comprising a DNA sequence which hybridizes to an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex, said DNA sequence being capable of hybridizing to a conserved region of said locus to allow determination of a HLA-DR- $\beta$  chain for use in HLA-DR- $\beta$  typing, said conserved region being encoded by a DNA sequence selected from the group consisting of:

- (i) DNA sequences encoding amino acids 39-45 of said locus, and

(ii) DNA sequences which are fully complementary to any of the foregoing DNA sequences.

101. An HLA-DR typing kit comprising a DNA sequence which hybridizes to an HLA-DR- $\beta$  chain locus of the human lymphocyte antigen complex, said DNA sequence being capable of hybridizing to a conserved region of said locus to allow determination of a HLA-DR- $\beta$  chain for use in HLA-DR- $\beta$  typing, said conserved region being encoded by a DNA sequence selected from the group consisting of:

- (i) DNA sequences encoding a majority of the amino acid sequence in a region consisting essentially of amino acids 39-45 of a polypeptide sequence coded for by DNA insert DR- $\beta$ -A, DR- $\beta$ -B or DR- $\beta$ -C, and
- (ii) DNA sequences which are fully complementary to any of the foregoing sequences.

102. The HLA-DR typing kit according to any one of claims 99, 100 or 101, wherein said DNA sequence is labeled.

REMARKS

The Claim Amendments